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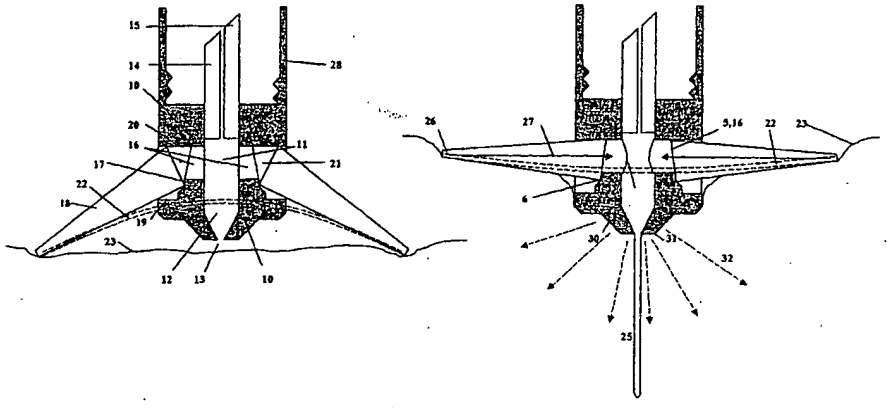
(54) Title: A LOW COST DISPOSABLE JET INJECTOR



(57) Abstract: A jet injector is described in which one or more end thrust beams impact on flexible portions of a rigid chamber between a nozzle and an extended constriction. The end thrust beams are driven by an over centre leaf spring that is energised by a pressure of the injector against the skin of the patient.

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A LOW COST DISPOSABLE JET INJECTOR

Jet injectors have been in use for more than fifty years. A high velocity jet of liquid drug passes through the skin and into the underlying tissue without need for a hypodermic needle. The procedure may be painless and far less intrusive than a standard injection. There no danger of accidental cross infection from contaminated sharps. More recently, disposable jet injectors have been devised which are driven by a small canister of compressed gas. These, however, are still more expensive than most injectable drug shots. There is a need for a jet injector of comparable cost to a hypodermic needle. There is also a need for a low cost jet injector that may be used for a number of shots from a single drug ampoule.

According to the present invention, there is a jet injector in which one or more end thrust beams may impact and depress corresponding flexible portions in the wall of a rigid chamber filled with liquid drug where the flexible portions of wall are sited between a nozzle and an extended constriction. The end thrust beam or end thrust beams are driven by an over centre spring which is preferably made of elastomeric material. The spring is compressed by pressing the injector against the skin of the patient. On passing through the central unstable equilibrium position, the spring accelerates the end thrust beam to impact with the flexible portion of wall. The geometry of the spring and flexible portion of wall may be adjusted so that the line of force of the spring lies approximately through the centre of the flexible portion of wall at impact. The spring is preferably in the form of two coplanar rigid end thrust beams, which bear on the rigid chamber at one end and are joined at their outer ends by two parallel leaf springs. Extended end surfaces on the end thrust beams at the rigid chamber end provide both a rotational bearing and a thruster element. The central gap between the end thrust beams is less than the spacing provided by the rigid chamber so that at rest the spring assembly is concave to the skin of the patient. On pressing the spring against the skin of the patient, the end thrust beams rotate about an axis approximately perpendicular to the skin of the patient axis so stretching the leaf springs until the spring assembly assumes the planar configuration of unstable equilibrium. The end thrust beams then accelerate rotationally to a configuration convex to the skin of the patient until the end thrust beams impact on the flexible portion of the rigid chamber wall. The impact force and residual spring tension raise the hydraulic pressure within the rigid chamber which accelerates a high speed liquid jet through the nozzle. Acceleration of fluid though the extended constriction is so

slow that little fluid escapes through the constriction during the high pressure transient. The jet cuts a track through the skin of the patient and the main dose of drug may be delivered via the unoccluded rigid chamber and track through the skin with a conventional piston and cylinder arrangement. Load need only be applied to the piston. If the nozzle cross sectional area is small compared with the piston, the pressure of the nozzle on the skin will provide a higher pressure hydraulic seal than the hydraulic pressure generated by the piston. If the spring tips press against the skin before the nozzle, any air in the pump may be preferentially expelled, prior to the formation of the hydraulic seal, due to the lower density of air compared with liquid drug. A pressure raising feature around the nozzle may pump away any extraneous lubricating fluid from the local nozzle skin interface and the resultant high frictional forces may retain the alignment of nozzle and track throughout the drug delivery.

Portable power sources are relatively expensive and complex. Power sources that may be used more than once, even more so. To reduce cost, this injector uses the pressure of the device against the skin of the patient to energise it. To reduce the power requirement, the main dose may be delivered manually with a piston and cylinder in the conventional fashion. This provides slow delivery which reduces soft tissue damage. The jet injector need only generate a single fast drop to cut a track through the skin.

The device comprises an over centre spring connected to one or more end thrust beams. The spring is stretched by pressure against the patient then on passing through the position of unstable equilibrium, accelerates the end thrust beams to impact with flexible portions within the wall of a rigid chamber. The impact and residual stress of the springs generate a high hydraulic pressure transient within the drug filled chamber. At one end the chamber tapers to a fine nozzle so that the pressure accelerates fluid through this nozzle to form a high speed liquid jet. This jet may cut a track through the skin. At the other end of the chamber is an elongated constriction. The high pressure transient will accelerate fluid through the constriction, but the fluid inertia is so great that liquid loss will be negligible for the duration of the transient. For low speed drug delivery, the constriction offers no significant resistance at all. The depression of the flexible portions of chamber is insufficient to occlude the chamber, so there is no need to retract the end thrust beam ends after firing. The main

dose of liquid drug may be fed through the jet injector by a piston and cylinder arrangement in the usual manner, then on through the track in the skin to the subcutaneous tissue.

The device may be held by the piston and pressed against the skin of the patient to actuate it. The force exerted on the piston will then also be exerted on the skin of the patient. If the cross sectional area of the piston is greater than the effective area of the nozzle, the hydraulic seal pressure against the skin must always be greater than that generated by the piston. A wet shot, in which drug flows partially over the outer skin of the patient, is therefore fundamentally impossible.

The track must clearly be kept accurately aligned with the nozzle throughout the drug delivery. Since the pressure on the skin will be continuous during delivery, there will be a continuous frictional force between the skin and the nozzle. If the nozzle is in the form of a truncated cone, tension in the skin will provide a very high and localised pressure loading along the circular locus of truncation. The localisation will ensure that any lubricating liquid film on the skin, such as drug or sweat, will rapidly be pumped away. The high pressure against dry skin will provide a localised high frictional retaining force which will maintain accurate registration of the nozzle and mouth of the track during drug delivery.

It is important that the track does not close during the duration of the shot. The conical form of the nozzle coupled with the pressure from the piston will place the skin under significant radial tension around the mouth of the track. This will keep the inlet to the track open for the duration of the shot and the delivery pressure will ensure that the remainder of the track also stays open.

It is important that the drug is delivered to the end of the track. The conical form of the nozzle will produce a radially decreasing stress pattern in the underlying tissues of approximately spherical symmetry. The compression of the soft tissues will tend to close the capillaries and the drug will be preferentially deposited at the end of the track.

The depth of shot can be precisely engineered. The initial jet will aggressively cut though the outer skin, but as the track develops, boundary layers will form in the flow pattern that will effectively progressively remove fluid from the jet. The boundary layer flow will be laminar due to the small scale and so may be very accurately predicted. By varying the cross section and duration of the jet, it will be possible to control the depth of the shot very accurately, irrespective of the toughness or thickness of the outer skin.

It is important that there is no back flow of drug out through the initial orifice. Unlike a normal injection the soft tissues are significantly compressed by the injection process. On removal of the injector, the soft tissue will relax and there will be a low pressure in the region of the injection rather than the conventional high pressure. There will, therefore be no tendency for outflow of the drug.

It is important the spring is robust in construction and accepts the energy of actuation within the material strain limits. It is found that it is effectively impossible to design an appropriate metal spring because of the high modulus and low yield strain. Polymeric materials have higher yield strain and lower moduli. High performance polymers such as PEEK, PSU and PES would seem ideal.

The base of the end thrust beam against the rigid chamber wall may be an extended surface that pivots. As the spring rotates, the line of action of the spring steadily moves away from the pivot point. It may be arranged the impact of the end thrust beam end surface with the flexible portion of chamber wall occurs when the line of action is approximately at its centre. In this manner, the residual spring force is instantaneously switched from the pivot point to the point of impact. In practice, this force will probably be double the impact loading, so is very significant.

The end thrust beam ends may be retained by sockets within the rigid chamber wall. By appropriately designing these sockets, they may set defined limits to the rotational travel of the end thrust beam, provide a land for the pivot action and control the movement of the flexible material.

The syringe may be flushed of air bubbles in the usual manner, prior to use, but the working volume of the effective injector pump is small and a slight spring back of the rubber syringe piston can induce inflow of air. Clearly bubbles within the pump will prevent correct operation. If it is arranged that the spring tips load the skin of the patient before the nozzle touches down, the syringe piston will flush any air from the pump chamber. Because the density of air is roughly one thousandth that of a liquid drug, acceleration of air through the nozzle will be rapid and escape of liquid drug will be negligible.

A preferred embodiment of the device is shown in figures 1 to 4. Figure 1 shows the spring in plan and elevation. Figure 2 shows the injection process in axial cross section through the rigid chamber. Figure 3 shows the external attachment. Figure 4 indicates retention of the end thrust beam in its socket.

A simple over centre leaf spring is used to store and release energy to drive the device. Figure 1 shows a typical spring, 1, in plan and elevation. There are two flexible leaf springs, 2, which are connected to rigid end thrust beams, 3, via a links, 4, that may undergo shear deformation during strain. The end thrust beams have extended central surfaces, 5, one corner of which, 6, acts as a rotational bearing and the surface, 5, provides the impact thrust.

Figure 2 shows a series of axial cross sections of the device during the injection cycle. In figure 2a, the device is shown prior to use. There is an injector body, 10, which comprises a rigid chamber, 11, a tapered section, 12, leading to a nozzle, 13, an elongated constriction, 14, which may lead to a piston and cylinder drug storage and delivery system. In this instance, the elongated constriction is a length of fine bore steel hypodermic chamber, which terminates in a sharp tip, 15, that may pierce the septum of a drug ampoule. The threaded end cap, 28, is provided to facilitate this. In other embodiments, the constriction may be cold formed or a welded constriction against a pin former. The rigid chamber, 11, also contains two flexible windows, 16, preferably moulded from silicone rubber and reference lands, 17.

The spring is shown in the initial configuration of concave to the skin of the patient. The end thrust beams, 18, bear on the reference lands, 17, and the front and rear walls,

19 and 20 respectively of a retaining channel, 21. The leaf springs, 22, are shown in dotted outline.

Figure 2a shows the assembly touching the skin of the patient, 23. The end thrust beam tips touch first the skin first and pressure on the piston expels any air from the pump chamber. As the density of air is roughly one thousandth that of water, acceleration of air through the nozzle is approximately a thousand times greater and requires very little pressure. Conversely, there will be minimal escape of liquid during the brief period.

Figure 2b shows upward deflection of the spring by pressure from the skin of the patient. The leaf springs flatten under load and extend elastically. The frusto conical nozzle embeds in the skin to form a hydraulic seal and registration device.

Figure 2c indicates the planar metastable configuration of the leaf springs, 22. There is still clearance between the thrust surfaces, 5, and the flexible windows, 16.

Figure 2d shows the moment after impact. The leaf springs, 22, are now convex with respect to the skin of the patient, 23. The extended end thrust beam surfaces, 5, have impacted with the flexible windows, 16, resulting in protrusion, 24, of the silicone rubber into the rigid chamber, 11. This results in the expulsion of a high speed jet, 25, through the skin of the patient, 23. The outer tips of the end thrust beams, 26, have moved sufficiently beyond the pivot point, 6, that the line of force, 27, lies approximately through the centre of the flexible windows, 16. The spring load is therefore transferred very rapidly from the pivot to the flexible window providing a very fast pressure rise time.

The main chamber is unrestricted by the displaced rubber so drug may now flow freely from the ampoule under the action of the piston to the end of the track cut in the skin of the patient.

The device may be simply re-cocked by manually pushing the spring forward to its initial position. In this manner, the device can be re-fired in the unlikely event of a

misfire. Such an event would be obvious to the user, as the piston would stay stationary. No leakage would occur as a wet shot, as explained above.

More significantly, the injector may be used for multiple metered deliveries from the same ampoule. This will have considerable significance for insulin delivery.

It is unlikely that both end thrust beams will impact simultaneously. However, the pressure required to shift both flexible windows and the intervening drug sideways is not very great and an effective single impact will occur when the second end thrust beam strikes.

The frusto conical nozzle, 30, is shown with the high pressure seal and frictional alignment retention along the locus of truncation, 31. The radially decreasing compressive stress distribution in the soft tissue is indicated by dotted lines, 32.

Figure 3 shows retention of the leaf springs, 22, by external detents on the injector body, 41. The position and profile of these detents may have a profound influence on the operation of the device. By arranging that the line of action of the spring tension, 42, is at an angle to the reaction from the rigid strut, 43, a number of important mechanical effects may be engineered. The mechanical advantage of the system can be engineered to produce a more linear force displacement curve for the spring, which may provide a lower skin loading for a given system energy. To obtain maximum residual pressure from the spring at impact requires, minimum distension of a very stiff spring. The mean mechanical advantage of the system can be increased by appropriate design of the detents. A modicum of pre tension in the spring will assist in retaining the end thrust beams in their sockets. With careful design, it may be ensured that a displaced spring tip will return automatically to the symmetrical disposition. It may even be arranged that both spring tips are automatically reset even if only one is pushed forward after firing.

Figure 4a shows the forces acting on the end thrust beams in regard to retention of the end thrust beam in its socket. Assuming zero friction, the reaction, 50, from the rear face, 20, to an applied load on the spring tip, 51, has a component along the strut, 52. The reaction, 53, from the forward wall has no such component. Under adverse

conditions, the strut will pop out of its retaining socket, 21. If a feature, 55, is added to provide a point or line contact with the forward wall, so that the line of the reaction force, 53, becomes parallel with reaction force, 50, it will cancel the pop-out component. Furthermore, the mechanical advantage of the leverage system ensures that reaction 53 is always greater than reaction 50, ensuring that the end thrust beam will stay in it socket..

The preferred material for the injector body and spring is polysulphone. It has medical certification, is highly stable, low mechanical loss, high yield strain, relatively low cost, is mouldable with mechanical properties that are substantially independent of the direction of melt flow. It is also very resistant to radiation damage which facilitates radiation sterilisation.

The preferred material for the rubber windows is medical grade silicone rubber, which is also very radiation resistant. Conventional silane primers are relatively ineffective on polysulphone but it is found that a 30% chlorobenzene addition does not affect the silanes but partially dissolves the polysulphone surface giving excellent adhesion. Any remaining solvent may be dispelled by heating before moulding.

If desired, a silicone non return valve may be moulded across the nozzle during the moulding of the flexible windows. Pierced silicone rubber tends to re-bond to itself with time. This problem may be circumvented by adding 20% silicone oil to the rubber before moulding. This does not impair the bonding of the flexible windows but it does permanently inhibit rebonding of a non return valve.

The nozzle may be in the form of a slot rather than the conventional circular nozzle. This offers the possibility of cutting a larger diameter track with less fluid energy which is desirable in terms of reducing skin loading.

It is possible to mould an intact silicone membrane across the nozzle to provide a hermetically sealed system for sterile storage. The membrane may be controllably burst with the high hydraulic pressure of the first firing. Forming a depression in the rubber with a triangular prism mould tool predisposes the membrane to burst in a controlled fashion, forming a jet along the mid plane of the prism.

CLAIMS

1. A jet injector comprising:

One or more end thrust beams actuated by a spring or springs, which are energised by pressure of the jet injector against the skin of the patient

A rigid chamber filled with liquid drug and comprising flexible portions within the chamber wall on which the end thrust beams may impact to generate a hydraulic pressure transient within the chamber

A nozzle outlet from the rigid chamber to produce a jet

A rigid hydraulic connection from the rigid chamber to a liquid drug supply via a constriction

2. A jet injector according to claim 1 in which the spring is made substantially from polymeric material.

3. A jet injector according to claim 1 wherein the spring comprises one or more end thrust beams which bear upon the rigid chamber at one end and are connected to each other or the rigid chamber via spring elements at the other such that rotation of the end thrust beams about axes approximately parallel to the skin of the patient at first strains the springs to a maximum stored energy then permits spontaneous reduction in strain with an associated rotational acceleration.

4. A jet injector according to claim 3 in which the end thrust beam ends have an extended surface that may pivot on the rigid chamber such that at impact with the flexible portion, the line of action of the spring force may lie substantially through the centre of the flexible portion.

5. A jet injector according to claim 4 in which there are two coplanar rigid end thrust beams operating about a parallel rotational axes with outer ends connected by two thin leaf springs disposed parallel to the rotational axis in which the connections may deform by shear and the leaf springs by extension.

6. A jet injector according to claim 5 in which the spring assembly is retained on the rigid chamber by detents which may be profiled to control the stability and load profile of the spring.

7. A jet injector according to claims 1 to 6 in which a manual piston and cylinder delivery is provided to deliver the main drug dose along the track cut though the skin of the patient by the high velocity jet

8. A jet injector according to claim 7 in which the operating load is applied to the piston alone.

9. A jet injector according to claim 8 in which the effective cross sectional area of the nozzle in contact with the skin is significantly less that the piston area, so that when a load is applied to the skin from the piston, the hydraulic seal between skin and nozzle will be proof to a higher hydraulic pressure than that generated by the piston.

10. A jet injector according to claims 1 to 6 in which load on the nozzle profile generates radial tension within the skin about the track entrance to hold it open during drug delivery.

11. A jet injector according to claims 1 to 9 wherein the nozzle profile incorporates a feature close to the outlet that generates a high local skin pressure such that extraneous fluid is pumped away from the feature and the high frictional force between the feature and the skin maintain registration of the nozzle outlet with the track cut through the skin during drug delivery.

Figure 1

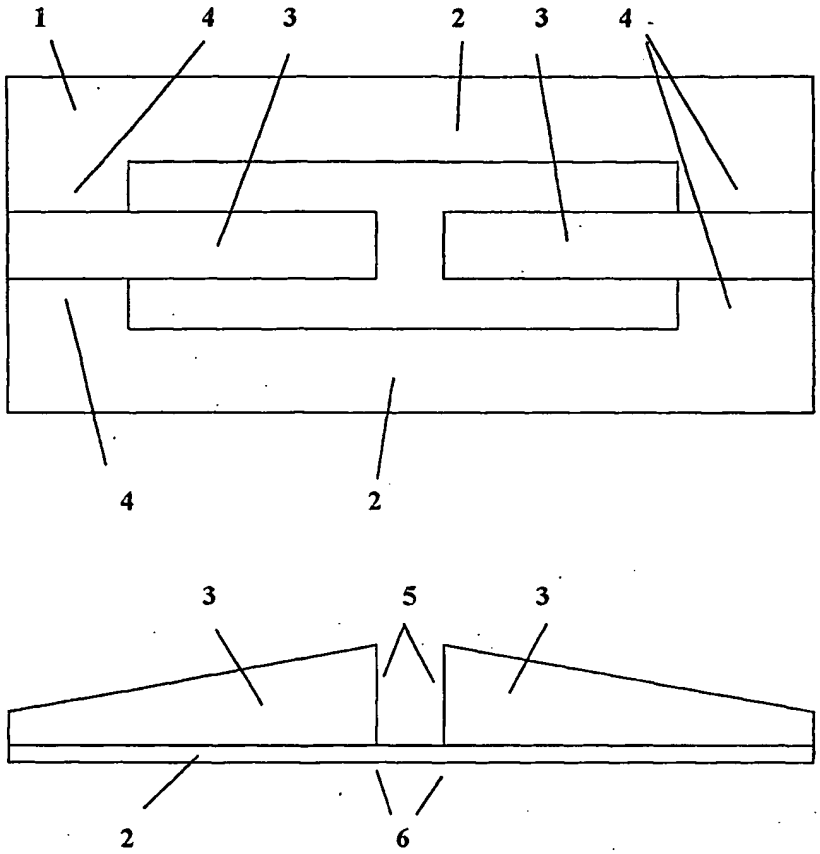


Figure 2

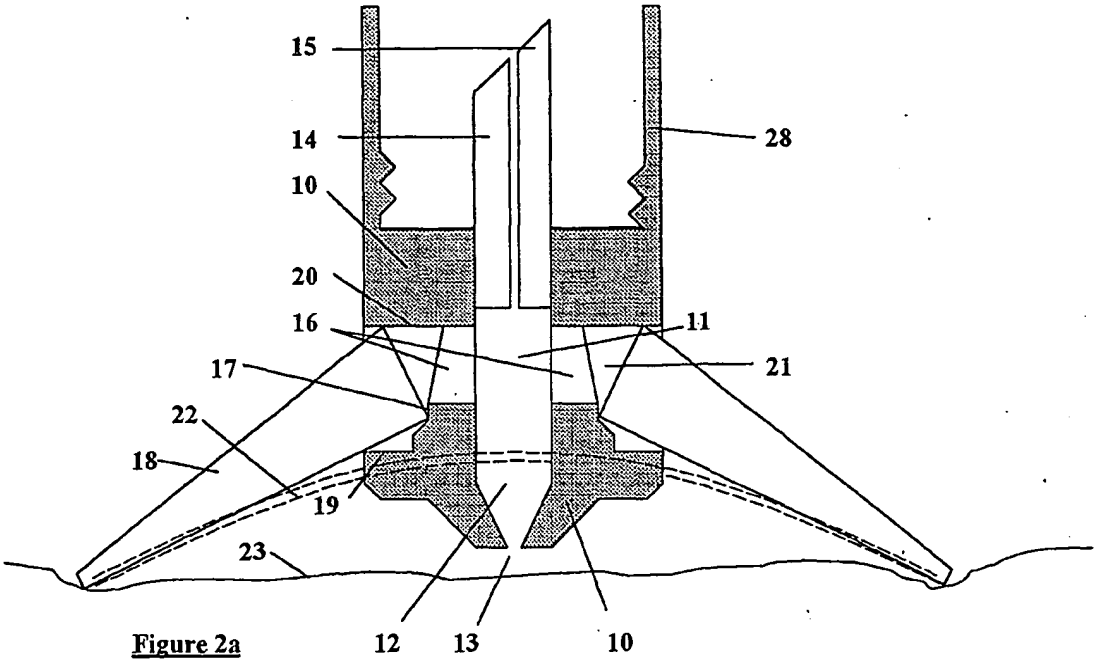


Figure 2a

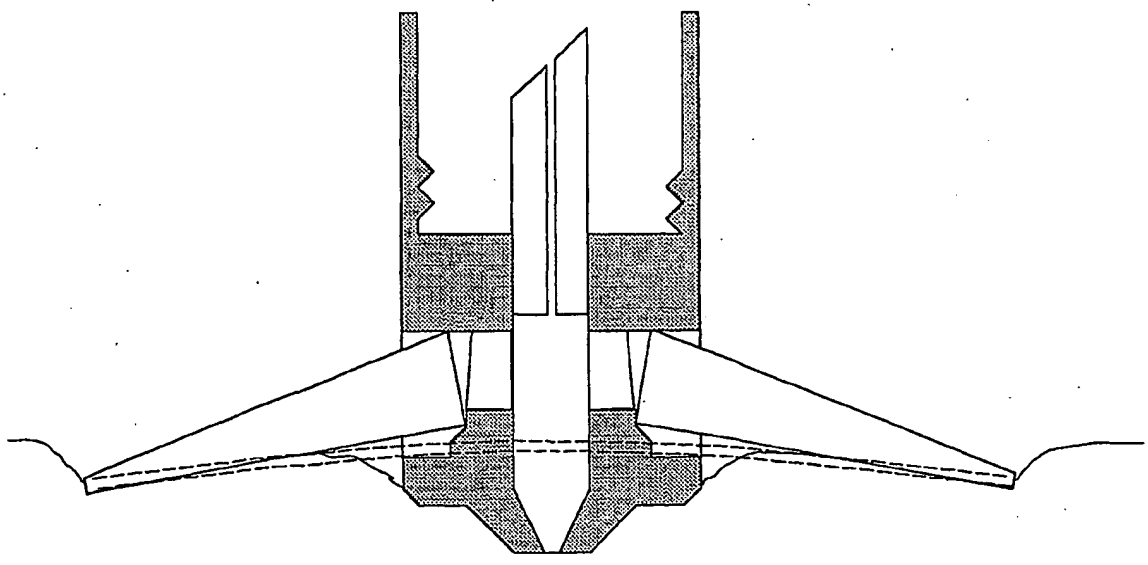


Figure 2b

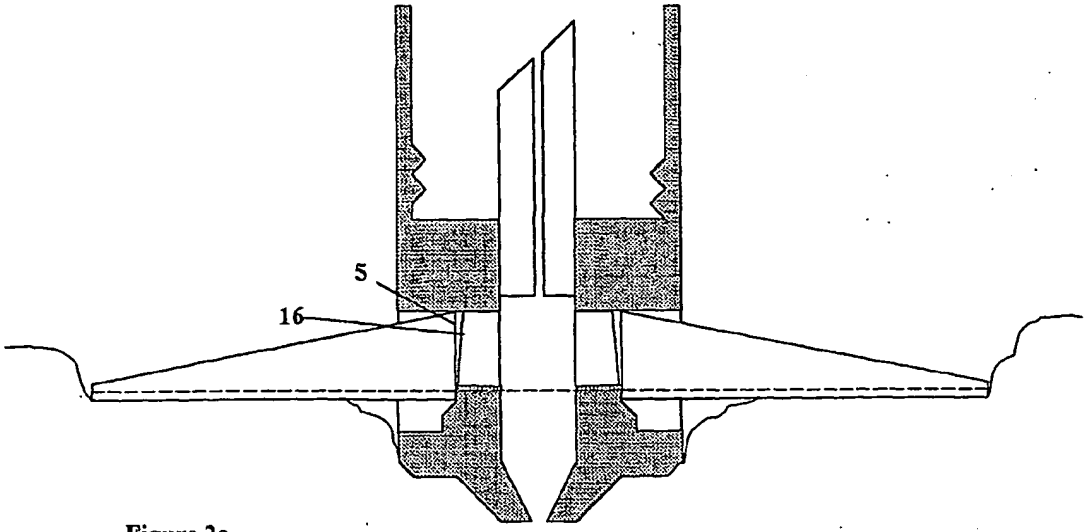


Figure 2c

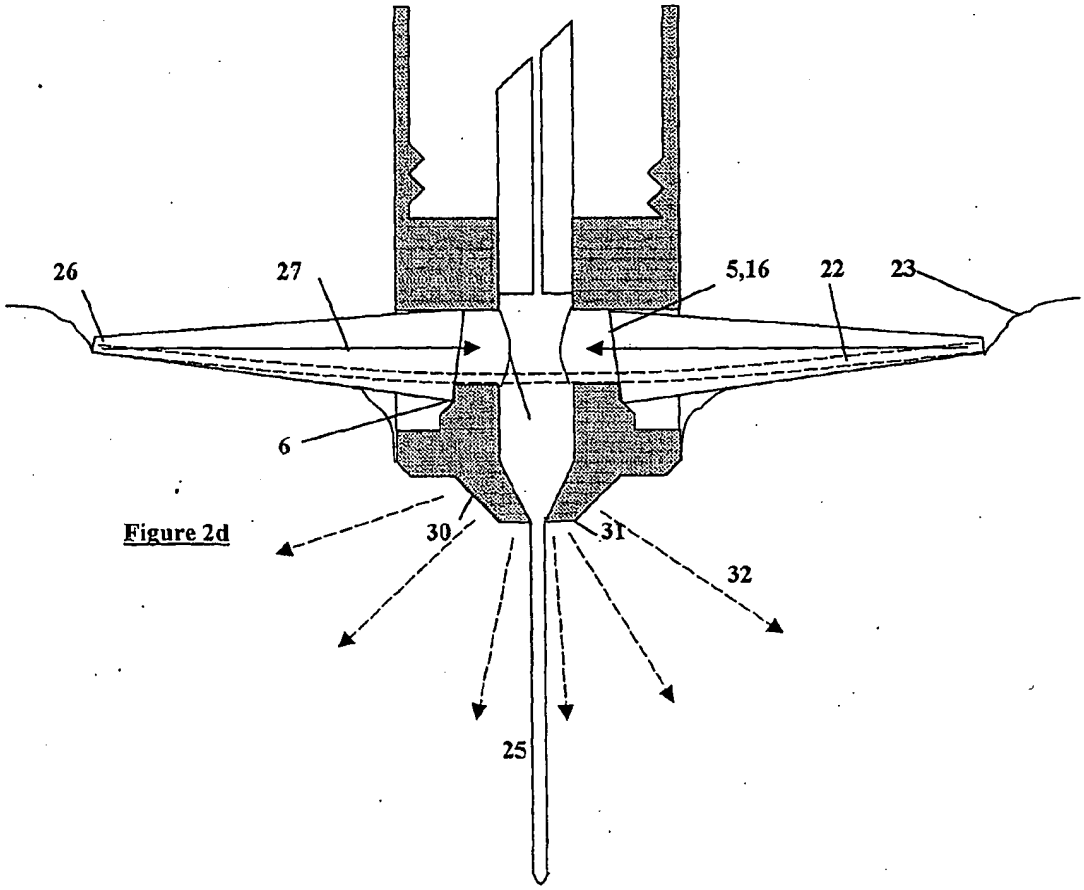
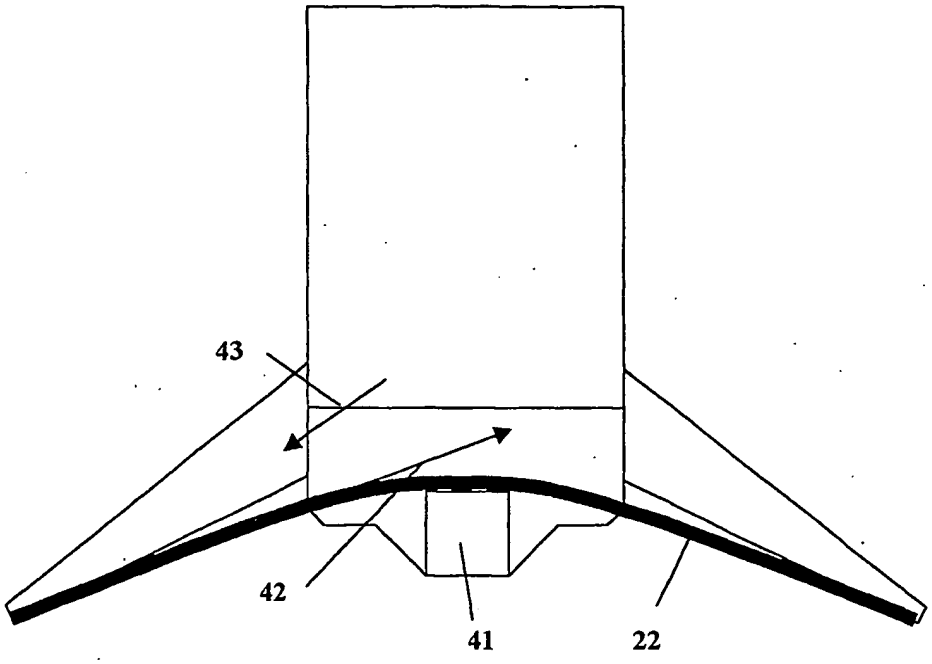


Figure 2d

Figure 3



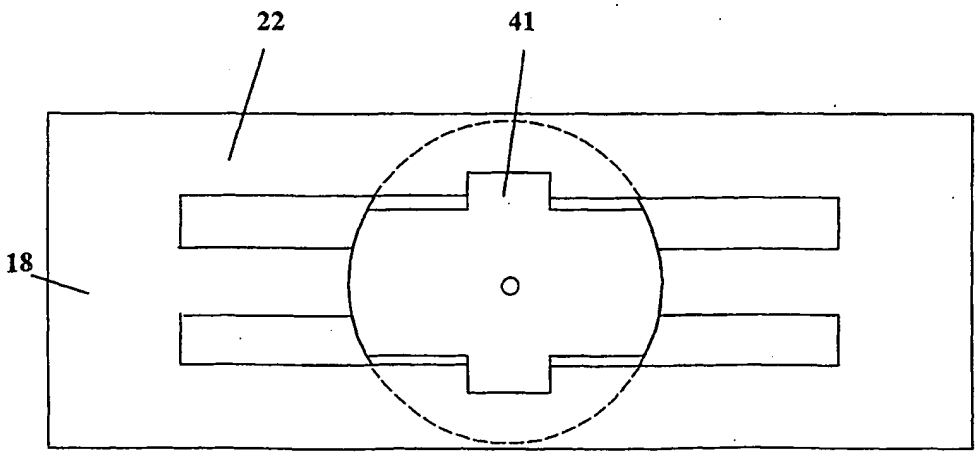
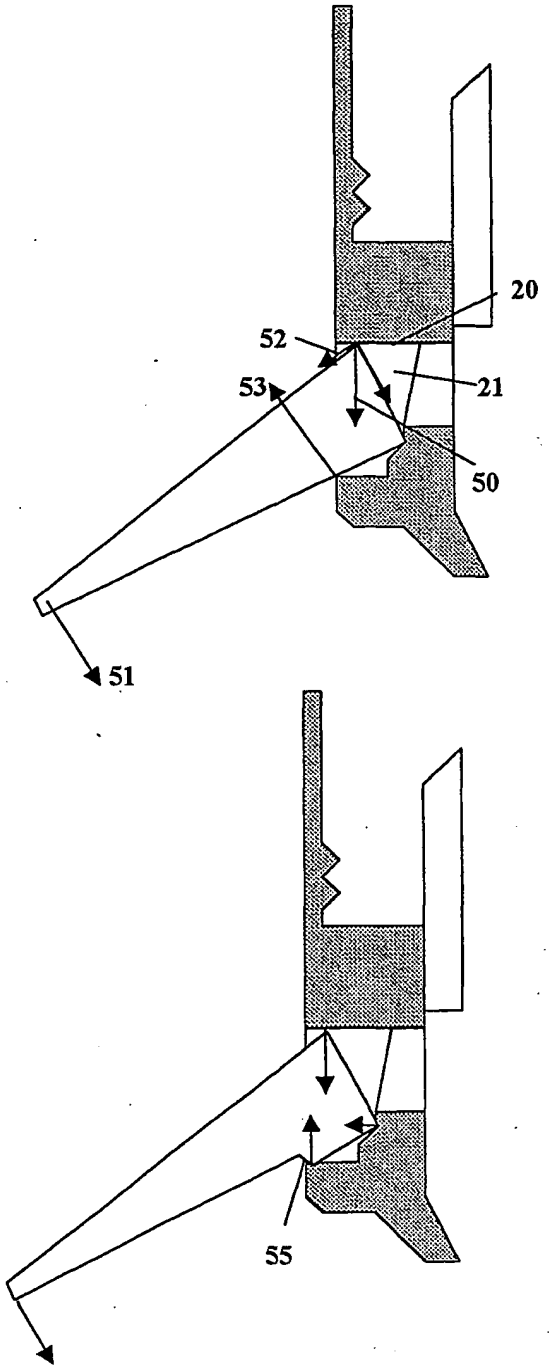


Figure 4



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 02/02633

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/30

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M B05C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A	US 5 034 003 A (DENANCE RAYMOND) 23 July 1991 (1991-07-23)	

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☒ Patent family members are listed in annex.

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22 October 2002	30/10/2002

Name and mailing address of the ISA	Authorized officer
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Information on patent family members

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